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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/783,083	02/15/2001	Avinoam Dukler	00/21362	3267

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EXAMINER

EPPERSON, JON D

ART UNIT PAPER NUMBER

1639

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/783,083

Applicant(s)

DUKLER ET AL.

Examiner

Jon D Epperson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 65-68, 70 and 72-88 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 65-68, 70 and 72-88 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

1. The Response filed September 23, 2004 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 65-74 were pending. Applicants canceled claims 69 and 71 and also added claims 75-88. In addition, Applicants amended claims 65, 66, 68, 70, 73 and 74 (see 5/13/04 Amendment). Therefore, claims 65-68, 70, 72-88 are currently pending.

Withdrawn Objections/Rejections

4. The Enablement Rejection under 35 U.S.C. § 112, first paragraph is withdrawn in view of Applicants' arguments and/or amendments. The 35 U.S.C. 112, second paragraph rejections denoted A and B are withdrawn in view of Applicants' arguments and/or amendments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

35 USC § 102 – Maintained Rejection

5. Claims 65, 68, 77, 78, 80, 81, 84-86 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al. (U.S. Patent No. 5,424,186) (Date of Patent is **June 13, 1995**).

For *claims 65, 80, 81 and 88*, Fodor et al. (see entire document) disclose a method for the directed spatially addressable “synthesis and use of diverse polymer sequences on a substrate” wherein a complex carbohydrate chip was formed (see Fodor, column 2, lines 32-33), which anticipates the above mentioned claims. For example, Fodor et al. disclose the production of complex polysaccharides on an addressable VLSIPS chip (has a plurality of addressable locations) using enzymatic synthesis such as a galactosyl transferase that generates an array of carbohydrates with at least two naturally occurring sugars (e.g., see Fodor et al., columns 68-69, Section V B, see especially column 69, paragraph 2; see also figures 40 A-E, especially figure 40 E; see also column 10, line 4 wherein “parallel” synthesis is disclosed). Fodor et al. do not explicitly state that the stereo-specificity of each bond interconnecting said monosaccharide units of said plurality of carbohydrate structures is defined by said addressable location. However, the Examiner contends that this would be an inherent feature as the enzymes used by Fodor et al. are identical to the enzymes used by Applicants and thus would be expected to produce “stereo-specific” products at the various locations on the chip (e.g., compare Fodor et al. column 69, line 6 to Applicants’ specification, figure 10a wherein galactosyl transferase is used in both cases). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant

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has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

For *claims 68 and 84*, Fodor et al. also disclose that the complex carbohydrates can be branched (e.g., see Fodor et al., column 16, lines 22-26, “Those of skill in the art will also note that more than one functional group can be employed on ... the monomer, i.e., to facilitate the synthesis of branched ... structures”; see also column 17, line 59; see also column 7, lines 35-48).

For *claims 77 and 85*, Fodor et al. disclose, for example, D-glucose (e.g., see Fodor et al., column 68, line 30).

For *claims 78 and 86*, Fodor et al. do not disclose whether or not the monosaccharide units are in the alpha or beta configuration. The reference is silent on the issue. However, the Examiner contends that Fodor et al. would inherently produce monosaccharides in either the alpha or beta configuration as the enzymes used by Fodor et al. are identical to the enzymes used by Applicants and thus would be expected to produce “stereo-specific” products at the various locations on the chip (e.g., compare Fodor et al. column 69, line 6 to Applicants’ specification, figure 10a wherein galactosyl transferase is used in both cases). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re*

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Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

In the alternative, the Examiner contends that the alpha and/or beta configuration would be “immediately envisioned” as there are only two possibilities that could occur from the use of the enzymatic synthesis disclosed by Fodor et al. For example, in *In re Schauman*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978), claims to a specific compound were anticipated because the prior art taught a generic formula embracing a limited number of compounds closely related to each other in structure and the properties possessed by the compound class of the prior art was that disclosed for the claimed compound. The broad generic formula seemed to describe an infinite number of compounds but claim 1 was limited to a structure with only one variable substituent R group. This substituent was limited to low alkyl radicals. One of ordinary skill in the art would at once envisage the subject matter within claim 1 of the reference disclosed in *In re Schauman*. Likewise, Fodor et al. disclose a formula (see Figure 40 E) that can have only two possibilities each of which would be immediately envisioned.

Response

6. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, “the teachings of U.S. Pat. No. 5,42,186 clearly focus on photo-activatable chemical synthesis and as such, not clear description or suggestion of complete synthesis of polysaccharides using enzymatic approaches is set forth in the document ... Since enzymatic reactions are highly specific both in branching patterns and stereo-specificity, a resultant carbohydrate population synthesized using such approach is uniform in both structure and stereo-specificity as opposed to the racemic mixture of carbohydrates of various branching patterns ... Thus, structural and stereo-specificity limitations of claim 65 and 70 and new claim 81 can only be attributed to a carbohydrate library which was fully synthesized using carefully planned enzymatic synthesis steps” (see 5/13/04 Response, page 8).

This is not found persuasive for the following reasons:

In response to applicants’ argument that the references fail to show certain features of applicant’s invention, it is noted that the features upon which applicant relies (i.e., “enzymatic synthesis”, “complete synthesis”, “carefully planned enzymatic synthesis steps”, “uniform in both structure and stereo-specificity as opposed to the racemic mixture”, etc.) are not recited in the rejected claim(s) i.e., claims 65 and 69. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Accordingly, the 35 U.S.C. § 102(b) rejection cited above is hereby maintained

New Rejections

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 65-68, 70, 72-87 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

In newly amended and/or added independent claims 65, 70 and 81 (e.g., see 5/13/04 Response), to the extent that the phrase “synthesizing a carbohydrate structure” extends beyond the previous limitation of “enzymatically” synthesizing a carbohydrate structure, the increased breadth of possible modification (i.e., deletion of the word enzymatically) constitutes new matter, since there is no specification support or original claim support for the full scope of the modification; nor has applicant provided any indication where such support exists for the full scope of the modification. Specifically, the Examiner does not find support for “synthesizing” a complex carbohydrate library via any other means than “enzymatic” synthesis. If applicant believes this rejection is in error, applicant must disclose where in the specification support for the full scope of this modification can be found. Therefore, claims 65, 70, 81 and all dependent claims are rejected as new matter.

8. Claims 65-68, 70, 72-87 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a few of the compounds that fall within the broad scope

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of the claimed invention (see below), is not enabling for the vast majority of compounds that fall within this broad scope. This is an enablement rejection.

Any person skilled in the art to which it pertains, or with which it is most nearly connected, would not know how to make and use the claimed invention. Applicant has not provided enough examples of how to make the claimed invention to be enabling for the full breadth of the claims. It is clear from applicant's specification how one might practice this invention using enzymatic synthesis to produce the stereo-specific carbohydrate array. However, applicant have not provided sufficient guidance as to how to make **any** of the stereospecific carbohydrate arrays without the use of enzymatic synthesis.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) Breadth of the claims and nature of the invention: Applicants' invention is not limited to enzymatic synthesis (see new matter rejection above). Thus Applicants

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claims read on an undefined number of methods both chemical and enzymatic for producing an array of carbohydrates. Consequently, the scope is broad and the nature of the claimed invention cannot be determined.

(3 and 5) The state of the prior art and the level of predictability in the art: The prior art provides only a few limited examples of carbohydrate arrays that have been stereospecifically synthesized (e.g., see the Fodor et al. 35 U.S.C. § 102 rejection for an example of enzymatic synthesis and Kahne et al. 35 U.S.C. § 102 rejection for an example of a chemical synthesis). In addition, Applicant admit on the record that the art is inherently unpredictable, if not impossible, when it comes to the stereospecific synthesis of carbohydrate arrays (e.g., see page 5/13/04 Response, page 8, third full paragraph, "Since enzymatic reactions are highly specific both in branching patterns and stereo-specificity, a resultant carbohydrate population synthesized using such an approach is uniform in both structure and stereo-specificity as opposed to the racemic mixture of carbohydrates of various branching patterns and stereospecificity that would result from chemical synthesis or a combined chemical-enzymatic synthesis").

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants specification does not provide any guidance for procuring stereospecific carbohydrate arrays with any other means other than enzymatic synthesis (e.g., see New Matter rejection above).

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(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 81 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claim 81**, the phrase “such that each addressable location supports a plurality of carbohydrate structures of identical structure and stereospecificity” is vague and indefinite. For example, it is not clear how “each” position can “support” more than one carbohydrate structure. It would appear to the Examiner that only “one” carbohydrate could be found at each addressable location, not a “plurality” of carbohydrates at each position. Applicants are requested to clarify and/or correct.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 65, 77, 78, 81, 85 and 86 are rejected under 35 U.S.C. 102(b) as being anticipated by Kahne et al. (WO 97/35202) (Date of Patent is **September 25, 1997**).

For **claims 65 and 81**, Kahne et al. (see entire document) disclose methods for the production of a carbohydrate ligand library (see Kahne et al., abstract), which anticipates the above-mentioned claims. For example, Kahne et al. disclose providing an array having a plurality of addressable location and synthesizing a carbohydrate structure on each of said plurality of addressable locations (e.g., see Kahn et al., page 1, Field of Invention, “The invention relates to a library of carbohydrate-based ligands, which are bound to and presented on a solid support [i.e., an array] to permit multivalent

interactions with a variety of probes having a plurality of carbohydrate binding sites”; see also page 20, lines 19-21, “... the library members can be arrayed on a planar support, such as a microtiter plate or glass slide”; see also page 18, lines 12-18 wherein “spatial addressing” is disclosed; see also figures 11-15; see also claims 1-2). Furthermore, Kahne et al. disclose “stereo-specific” synthesis at these positions (e.g., see Kahne et al., page 21, last paragraph, “the glycosylation method used should preferably achieve glycosylation stereospecifically for all the different donor/acceptor pairs”; see also page 29, lines 18-21, “The sulfoxide glycosylation reaction proceeds stereospecifically and in near quantitative yield”). Finally, Kahne et al. disclose the generating carbohydrate structures between 2 and 20 carbohydrates that are composed of “natural” monosaccharides (e.g., see page 22, lines 30-31, “The exemplified library is designed to include the natural ligand for peanut agglutinin”; see also figures 10, 12 and 13 and compounds showing “natural” monosaccharides therein; see also page 11, lines 35-36; see also page 96, last paragraph).

For *claims 77 and 85*, Kahne et al. disclose, for example, D-Galactose (e.g., see figure 13).

For *claim 78 and 86*, Kahne et al. do not disclose whether or not the monosaccharide units are in the alpha or beta configuration. The reference is silent on the issue. However, the Examiner contends that Kahne et al. would inherently produce monosaccharides in either the alpha or beta configuration as the reactions are stereospecific (e.g., see Kahne et al., page 21, last paragraph, “the glycosylation method used should preferably achieve glycosylation stereospecifically for all the different

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donor/acceptor pairs”; see also page 29, lines 18-21, “The sulfoxide glycosylation reaction proceeds stereospecifically and in near quantitative yield”). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

In the alternative, the Examiner contends that the alpha and/or beta configuration would be “immediately envisioned” as there are only two possibilities that could occur from the use of the enzymatic synthesis disclosed by Fodor et al. For example, in *In re Schauman*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978), claims to a specific compound were anticipated because the prior art taught a generic formula embracing a limited number of compounds closely related to each other in structure and the properties possessed by the compound class of the prior art was that disclosed for the claimed compound. The broad generic formula seemed to describe an infinite number of compounds but claim 1 was limited to a structure with only one variable substituent R group. This substituent was limited to low alkyl radicals. One of ordinary skill in the art would at once envisage the subject matter within claim 1 of the reference disclosed in *In re Schauman*. Likewise, Fodor et al. disclose a formula (see Figure 40 E) that can have only two possibilities each of which would be immediately envisioned.

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Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
December 28, 2004

BENNETT GELSA
PRIMARY EXAMINER

